Mitochondrial DNA Variation and Disease Susceptibility in Primary Open-Angle Glaucoma

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PURPOSE: To determine whether mitochondrial DNA haplogroups or rare variants associate with primary open-angle glaucoma in subjects of European descent.

METHODS: A case-control comparison of age- and sex-matched cohorts of 90 primary open-angle glaucoma patients and 95 population controls. Full mitochondrial DNA sequences from peripheral blood were generated by next-generation sequencing and compared to the revised Cambridge Reference Sequence to define mitochondrial haplogroups and variants.

RESULTS: Most subjects were of the major European haplogroups H, J, K, U, and T. Logistic regression analysis showed haplogroup U to be significantly underrepresented in male primary open-angle glaucoma subjects (odds ratio 0.25; 95% confidence interval http://CI 0.09-0.67; P = 0.007; Bonferroni multiple testing P = 0.022). Variants in the mitochondrial DNA gene MT-ND2 were overrepresented in the control group (P = 0.005; Bonferroni multiple testing correction P = 0.015).

CONCLUSIONS: Mitochondrial DNA ancestral lineages modulate the risk for primary open-angle glaucoma in populations of European descent. Haplogroup U and rare variants in the mitochondrial DNA-encoded MT-ND2 gene may be protective against primary open-angle glaucoma. Larger studies are warranted to explore haplogroup associations with disease risk in different ethnic groups and define biomarkers of primary open-angle glaucoma endophenotypes to target therapeutic strategies.